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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BAKER BOTTS L.L.P. 30 ROCKEFELLER PLAZA 44TH FLOOR NEW YORK, NY 10112-4498			EXAMINER DEJONG, ERIC S	
			ART UNIT 1631	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Office Action Summary	Application No. 10/073,463	Applicant(s) RZHETSKY ET AL.	
	Examiner Eric S. DeJong	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18, 19, 21, 25-29, 31-33 and 36-45 is/are pending in the application.
- 4a) Of the above claim(s) 18, 19, 21, 25-29 and 31-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED OFFICE ACTION

As set forth in the Pre-Brief Appeal Conference decision, mailed 09/05/2007, the finality of the previous Office action is withdrawn and a new Office action on the merits is provided herein.

Claims 1-17, 20, 22-24, 30, 34, and 35 are canceled. Claims 18, 19, 21, 25-29, 31-33, and 36-45 are pending in the instant application. Claims 18, 19, 21, 25-29, and 31-33 are withdrawn as being drawn to a non-elected invention (see the Office action mailed 06/28/2006). Claims 36-45 are currently under examination.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See for example paragraph 0032, 0044, and 0056 of the instant specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claim 38 is objected to because of the following informalities:

Claim 38, line 16 recites phrase "the identification of molecular interaction corresponding to" and should be amended to read as --the identification of ***the*** molecular interaction corresponding to-- (emphasis added).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The previous rejection of claims 36-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite set for in the previous Office action, mailed 04/16/2007, is withdrawn in view of arguments presented by applicants.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36, 37, and 39-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 recites the use of "equation 10" in line 32. Similarly, claim 39 recites the use of "equation 6 or 14", claim 40 recites the use of "equation 14", claim 41 recites the use of "equations 5 or 17", and claim 42 recites the use of "equation 17". It is acknowledged that the instant specification does disclose equations labeled 5, 6, 10, 14, and 17 and the terms recited therein. However, it is unclear whether the labeled equations of the specification are indeed those referred to in the claims. In addition, MPEP 2173.05(s) states that where possible, claims are to be complete in themselves and incorporation by reference to the specification to specific figures or tables is permitted only in exceptional cases and where it is more concise to incorporate by reference the duplicate drawing or table in the claim. Equations 5, 6, 10, 14, and 17 are represented in the specification as single line of text and, therefore, do not present an exceptional case that justifies the incorporation by reference of said equations into the

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instant claims. Claim 37 is also included under this rejection due to its dependence from claim 36.

For the benefit of applicants, this rejection could be overcome by an amendment to the instant claims to recite the equations identified above and the definitions of the terms used therein.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 36-45 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 36-45 are drawn to a method for identifying a molecular interaction network representation for a set of interacting molecules within a known biological system. The process for identifying a molecular interaction network representation involves abstract and computational steps for the determination of attraction probabilities, an edge probability, a network topology, and a network probability for said set of interacting molecules and, therefore, involves the application of a judicial exception. Regarding inventions involving the application of a judicial exception, said application must be a practical application of the judicial exception that includes either a step of a physical transformation, or produces a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447

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(1999)). In the instant claims, there is no step of physical transformation, thus the Examiner must determine if said application of a judicial exception produces a useful, concrete, and tangible result.

A tangible result requires that the claim must set forth a practical application of a judicial exception to produce a real-world result. It is acknowledged that instant claim 36 further recites a step of identifying the possible molecular interaction network having the highest posterior probability, however this step does not require any output, display or communication of a result of the method (an identified molecular interaction network) to a practitioner. Therefore, said claim lacks a tangible, real world result. It is further acknowledged that claim 38 has been amended to recite a step of providing the identification of a molecular interaction corresponding to the highest of the determined molecular interaction probabilities to a user or further processor. While the output of a result (an identified molecular interaction) to a user does provide a tangible, real-world result, the alternative embodiment recited in the instant claim wherein a result is provided to a further processor does not require any output, display or communication of a result to a practitioner in a tangible, real world context. As such, claim 38 still reads on embodiments that encompass non-statutory subject matter. Claim 37, which depends from claim 36, and claims 39-45, which depend from claim 38, are also included under this rejection because said dependent claims do not further limit either of claims 36 or 38 to only statutory embodiments.

Response to Arguments

Applicant's arguments filed 07/16/2007 have been fully considered but they are not persuasive.

In regard to the rejection of claims under 35 USC § 101 as being drawn to non-statutory subject matter, applicants argue that the instant claims conform to requirements of 35 USC § 101 without an express "providing to user" clause which applicants representative's experience/understanding is no longer required by the USPTO (see page 5 of applicants response filed 07/16/2007).

In response, it is noted that MPEP § 2106 sets forth the current guidelines for analysis of claims for statutory subject matter, which is relied upon as the basis for the instant rejection. It is also noted that an express "providing to user" clause is not a requirement in all statutory process claims, but rather one example of how a claim that recites only abstract process steps can provide a result that is considered a practical application. In order to satisfy this practical application requirement, a claim must include either a step of a physical transformation, or produce a useful, concrete, and tangible result (see especially MPEP 2106(IV)(C)). Since the instant claims do not include a step of physical transformation nor are limited to statutory embodiments; e.g. producing a concrete, tangible, and useful result, said claims do not meet the requirements of 35 USC §101.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 38 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Eisenberg et al. (US Patent No. 6,772,069).

The instant claims are drawn to a method for identifying a molecular interaction of a molecule within a biological network of interacting molecules comprising the steps of identifying a conserved feature of said molecule, determining probabilities of attraction between the conserved features and other interacting molecules based on known molecular interaction data, determining probabilities of molecular interaction of said molecules with each other interacting molecules based on the attraction probabilities, identifying the molecular interaction of said molecule corresponding to the determined probabilities of molecular interactions and providing the identification of the molecular interaction corresponding to the highest determined molecular interaction probabilities to a user or further processor.

Eisenberg et al. sets forth a computational method, system and computer program for inferring functional links from conserved genomic sequences (see Eisenberg et al., Abstract). Eisenberg et al. teaches the comparison of conserved

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genomic sequences to identify single protein chain sequences (Rosetta Stone sequences) that are further relied upon to determine interactions between protein components (see Eisenberg et al., Figure 11 and col. 3, lines 1-17 and lines 36-47), which reads on identifying a conserved feature of a molecule within a biological network, as recited in claim 38, and conserved features of a protein domain, as recited in claim 43. Eisenberg et al. further discloses the determination of the distance between two proteins by comparing the phylogenetic profiles of different proteins. This process includes constructing a conditional probability matrix, $p(aa \rightarrow aa')$, for proteins within a family that are grouped together on the basis of sequence homology (see Eisenberg et al. col. 4, lines 18-67), which reads on the determination of probabilities of attraction between conserved features of said molecule and other interacting molecules based on molecular interaction data as recited in claim 38. Eisenberg et al. further discloses accounting for conserved alignment in the constructed conditional probability matrix by taking the product of the conditional probabilities for each aligned pair of sequence using the equation $P(p) = \prod p(aa_n \rightarrow aa'_n)$ (see Eisenberg et al., col.4, lines 42-67), which reads on determining the probability of molecular interaction based on the probabilities of attraction as recited in claim 38. Eisenberg et al. further discloses the subsequent determination of a distance a from powers equation $p'=p^a (aa \rightarrow aa')$ and maximizing for P in the above equation for $P(p)$, which reads on the identification of said molecule corresponding to the highest determined probabilities of molecular interactions as recited in claim 38. Eisenberg et al. further discloses exemplary results from applications of the above described method (see Eisenberg et al., Table III and col. 26,

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line 13 through col. 29, line 6), which reads on providing the identification of a molecular interaction corresponding to the highest determined molecular interaction probability to a user as recited in claim 38.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 36-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eisenberg et al. (US Patent No. 6,772,069) as applied to claims 38 and 43 above, and further in view of Askenazi et al. (US Patent No. 6,594,587, see the references cited by the examiner mailed 11/15/2004) and in view of Friend et al. (US Patent No. 6,203,987), as evidenced by Perlin (US Patent No. 5,604,100).

The instant claims are drawn to related methods for identifying a molecular interaction of a molecule within a biological network of interacting molecules comprising determining attraction probabilities between pairs of molecules based on known molecular interaction data, determining an edge probability $P(E)$, which is the probability of a single network having a particular edge set, for each possible network interaction of a set of interacting molecules, determining a network topology $P(\text{topology})$, which is the probability that a network has a particular distributions of edges for a given vertex, based on the possible molecular interactions for a given network, determining a network probability for each molecular interaction as a product of said edge probability and topology probability, determining a posterior probability of for each molecular interaction network, and identifying the possible molecular interaction having the highest posterior probability. Further recited embodiments include the use of equation 10 for determining posterior probability, the use of equations 6 and 14 for determining attraction probabilities, the use of equations 5 and 17 for determining molecular probability of interaction, and further introducing a compound into a biological network and determining if the compound is being capable of modifying the interaction between molecules in a given network.

As discussed above, Eisenberg et al. sets forth a computational method, system and computer program for identifying functional links and conserved genomic sequences to identify conserved protein sequences and interactions between protein components (see Eisenberg et al., Abstract and col. 3, lines 1-17 and lines 36-47). However, Eisenberg et al. does not teach the determination of an edge probability, a

network topology probability, a network probability, a posterior probability, or the use of equations 5, 6, 10, 14, and 17 as recited in claims 36, 37, and 39-42. Further, Eisenberg et al. does not teach the use of the disclosed method for testing whether a compound is capable of modifying the interaction between at least two molecules in a biology network as recited in claims 44 and 45.

Askenazi sets forth a robust method for determining associations among a set of biological elements using algorithms for generating a Steiner tree, which is a network representation of associated biological elements (see Askenazi, Abstract, Figure 1, and col. 6, line 5 through col. 7, line 15). The disclosed method comprises computationally deriving relationships among a set of biological elements, wherein the biological elements are represented as vertices and the interactive relationships between said biological elements are represented as edges (see Askenazi, col. 2, lines 30-52). Askenazi further discloses embodiments wherein vertices represent enzymes (proteins) and substrates and wherein edges represent enzyme-enzyme and substrate-enzyme interactions (see col. 5, lines 42-61). The representation of associations between biological elements is taught as a heuristic modeling approach that results in the determination of the most efficient connection between vertices and edges of the graph corresponding to a "Context Set" (see especially Askenazi, col. 6, line 57 through col. 7, line 3). Askenazi further teaches that the output of the disclosed method is a "Steiner subgraph", which is a combination of a plurality of Steiner Trees solutions all having the same number of edges and vertices and edges (see Askenazi, col. 7, lines 4-15).

While Eisenberg et al. teaches the above described method for identifying functional links between conserved protein sequences and identifying interactions between protein components and Askenazi teaches a method for determining associations among a set of biological elements, neither Eisenberg et al. nor Askenazi teach the use of equations 5, 6, 10, 14, and 17 as recited in claims 36, 37, 39-42. Further, neither Eisenberg et al. nor Askenazi teach the use of the disclosed method for testing whether a compound is capable of modifying the interaction between at least two molecules in a biology network as recited in claims 44 and 45.

Friend et al. sets forth methods for enhanced detection of biological response patterns, classifying cellular constituents, such as measurable protein activities, into groups based upon the covariation among said constituents, and drug discovery (see Friend et al., Abstract and col. 2, lines 21-41). Friend et al. discloses embodiments of the method wherein statistical algorithms are relied to derive a "clustering tree" to model resultant patterns between related cellular constituents in response to cellular perturbations (see Friend et al., col. 1, lines 51-62 and col. 2, line 42 through col. 3, line 12). Friend et al. further specifies embodiments that rely upon objective statistical tests to define truly distinct branches within a clustering tree derived from a Monte Carlo modeling approach. While Friend et al. does not expressly teach the use of equations 5, 6, 10, 14, and 17 to determine posterior probability, attraction probabilities, molecular probability of interaction, said equations are taught by the instant specification as being derived from known statistical Monte Carlo sampling methods (see paragraph 0006 of the instant specification). Perlin is relied upon in the instant rejection as providing

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evidence that Markov chain Monte Carlo statistical techniques in Bayesian network approaches are well known in the art as being applied to the modeling biological systems (see Perlin, col. 16, lines 52-63). One of ordinary skill in the art would recognize that known applications of Markov chain Monte Carlo statistical techniques would have yielded predictable results and, further, would have resulted in the derivation and use of equations 5, 6, 10, 14, and 17 as instantly claimed. Friend et al. further discloses illustrative drug discovery applications wherein a drug candidate (test compound) is introduced into a model of cellular constituents (see Friend et al., col. 17, line 8 through col. 18, line 44). Following the introduction of a drug, the resultant perturbations to the model of cellular constituents is relied upon to evaluate (screen) the potential efficacy of said drug.

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to combine the method for identifying functional links and interactions between conserved protein sequences, as taught by Eisenberg et al., the method for determining associations among a set of biological elements wherein said biological elements are represented as vertices and interactive relationships between said biological elements are represented as edges, as taught by Askenazi, and the method for enhanced detection of biological response patterns and classifying cellular constituents into groups based upon the covariation among said constituents, as taught by Friend et al., to arrive at the instantly recited methods for identifying a molecular interaction network representation. One of ordinary skill in the art could have combined the known methods disclosed in the prior

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art to yield a predictable result because each of said methods performs the same function either separately or in combination.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Moran Marjorie can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MARJORIE A. MORAN
SUPERVISORY PATENT EXAMINER

Marjorie A. Moran
11/13/07

Eric S DeJong
Examiner
Art Unit 1631